

January 24, 2018

Title of the study:

## **BIOAVAILABILITY OF PHYTOESTROGENS AND PREVALENCE OF COLON POLYPS (FITOPOL)**

This document is relevant to the study in the record

The NCT number is not yet available

**INTRODUCTION:** Data obtained by *in vitro* and *in vivo* studies have demonstrated that phytoestrogens have an inhibitory effect on colorectal cancer (CRC). In humans, most of the studies on the influence of phytoestrogens in CRC, coming from population studies comparing the dietary intake of phytoestrogens, have produced contrasting results (1-5). The variability of these data may be essentially due to three different aspects: 1) phytoestrogens include several subclasses that differ for their preventative effects against CRC and colon adenomas; 2) the real absorption of phytoestrogens (by a serum or urinary determinations) is strongly influenced by the intestinal microbiota; 3) the production of equol, which is the most active phytoestrogen molecule, has not been determined.

**PURPOSE:** To evaluate phytoestrogen absorption and equol production in individuals with and without colonoscopy-proved colonic adenoma. Moreover, the prominent genera of the human microbiome potentially involved in equol production was evaluated.

### **STUDY DISEGN:**

Patients who underwent colonoscopy that demonstrated the presence of sporadic colorectal adenomas (Group I, case) or the absence of sporadic colorectal adenomas (Group II, control), matched for sex, age and BMI, will participate to the study. For the enrolment, they had to be undergone colonoscopy within the previous 1-3 months. In these patients we will evaluate: BMI, dietary history (for quantitative and qualitative analysis of dietary habits), quantitative analysis of phytoestrogens (by dietary questionnaires), home-based medications (aspirin), characteristics polyps (for calculating the risk of cancer), quantitative analysis of urinary excretion of phytoestrogens [by high pressure liquid chromatography (HPLC)] and intestinal flora [by mass spectrometry with Matrix Assisted Laser Desorption Ionization Time-of-Flight (MALDI-TOF) technology].

At the enrolment, patients will be invited to assume a standard quantitative of phytoestrogens at 8:00 a.m. and collect both a fecal sample and the urine of the following 24 hrs.

Inclusion criteria:

- subjects of both sexes aged between 50 and 75 years.

Exclusion criteria:

- age < 50 and > 75 years
- previous diagnosis of colon cancer or inflammatory bowel diseases (IBD)
- Hereditary intestinal tumors (FAP, HNPCC, ...)
- ongoing infections
- intake, in the last 4 weeks, of drugs that could alter the intestinal microflora
- creatinine clearance below 60 ml/min
- liver failure

## REFERENCES:

- 1) Jin H, Leng Q, Li C. Dietary flavonoid for preventing colorectal neoplasms. Cochrane Database Syst Rev. 2012;15:CD009350
- 2) Kocic B, Kitic D, Brankovic S. Dietary flavonoid intake and colorectal cancer risk: evidence from human population studies. J BUON. 2013;18:34-43
- 3) Xu X, Harris KS, Wang HJ, Murphy PA, Hendrich S. Bioavailability of soyben isoflavones depends upon gut microflora in women. J Nutr 1995;125:2307-2315
- 4) Atkinson C, Frankenfeld CL, Lampe JW. Gut bacterial metabolism of the soy isoflavone daidzein: exploring the relevance to human health. Exp Biol Med (Maywood) 2005;230:155-170.
- 5) Setchell KD, Brown NM, Lydeking-Olsen E. The clinical importance of the metabolite equol-a clue to the effectiveness of soy and its isoflavones. J Nutr. 2002;132:3577-84

## **STATISTICAL ANALYSIS PLAN**

Continuous variables will be expressed as means  $\pm$  standard deviation. The t test for unpaired data (age and body mass index) will be used. The categorical variables (i.e. gender, proportion of specific bacterial genera in the feces, etc.) will be analyzed using the Chi-square or Fischer test (one- or two-tailed). For statistical analysis, SPSS software version 21.0 will be used.

## INFORMED CONSENT

**TITLE OF THE STUDY:** Bioavailability of phytoestrogens and prevalence of colon polyps

### **1. Introduction**

In this center a clinical trial is being carried out and you are invited to take part of it. Before you decide, it is important that you understand why the trial is being conducted and what it will entail. Please take your time to read this information and consult your family doctor if you wish. Furthermore, as this form may contain words that are difficult to understand, ask the doctor responsible for the study or a doctor of your choice for any explanation or information that you deem appropriate. Take your time to decide if you want to participate.

### **2. What is the aim of the study?**

- Primary objective: to evaluate whether patients with low urinary excretion of phytoestrogens (and therefore with reduced absorption of phytoestrogens) have a higher incidence of colon polyps.
- Secondary objective: to identify the intestinal microbiota that best metabolizes the phytoestrogens.

### **3. Why do you have been chosen?**

You were invited to participate in this study because you were considered suitable; in fact, you were chosen because you are on the list for performing a colonoscopy and you are between 50 and 75 years old.

### **4. Am I bound to participate?**

Your participation in this study is completely voluntary.

If you decide to participate, you will be asked to sign a consent form, and you will be given a copy of this document to keep.

If you decide to participate, you are still free to stop your participation at any time without giving any explanation.

The decision not to participate in the study or to stop participating will have no impact on the medical treatment you will receive.

### **5. What will happen if I decide to participate?**

Fifteen days before the colonoscopy, you will be asked to provide a sample of your stool and urine after taking a specific amount of phytoestrogens. Moreover, you will be asked to answer a dietary questionnaire.

### **6. What are the possible benefits of participating to the study?**

The results of this study could contribute to distinguish patients with low or high incidence of colon polyps on the basis on their ability to absorb phytoestrogens from the diet.

### **7. Who reviewed the study?**

This study has been reviewed and approved by the "ETHICAL COMMITTEE OF THE POLYCLINIC HOSPITAL OF BARI". Thank you for reading this document and if you have any further doubt or questions, please contact the doctor responsible for the study.

Your participation in this study is very useful for us and we thank you in advance if you decide to participate.

The data will be processed in accordance with the Legislative Decree 196/03.

At any time during the study, you can request further information to:

the doctor responsible for the study

Dr. ....

Tel: .....

Date \_\_\_\_\_